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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/656,364	09/06/2000	Alice C. Martino	6107.N CN2	3730

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/656,364	MARTINO ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-20,22-24,26,34,36,68,70 and 71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-20,22-24,26,34,36,68,70 and 71* is/are rejected.

7)☒ Claim(s) *70 and 71* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/17/05*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 17, 2005 has been entered.

Claims 2-20, 22-24, 26, 34, 36, 68, 70-71 are pending

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 2-20, 22-24, 26, 34, 36, 68 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 6,177,101. Although the conflicting claims are not identical, they are not patentably distinct from each other because they overlap in scope.

The patented claims are directed to non-sustained release, non-chewable tablets comprising delavirdine mesylate as the sole active ingredient, microcrystalline cellulose, a polymeric binder, and a superdisintegrant. The claimed invention comprise of the same ingredients except the language of delavirdine is replaced by a the recitation of "a rapidly precipitating drug which is a fairly soluble or highly soluble salt form of a poorly soluble free base or free acid that is prone to supersaturating when introduced in water or simulated physiological fluid at body temperature and more than 90% of it precipitates out within 60 min after coming into contact with said water of simulated physiological fluid at body temperature, with the provisio that the drug is not delavirdine mesylate." Since delavirdine falls within the instantly claimed generic group of compounds, it would have been obvious to one of ordinary skill in the art at the time of invention to use other such active compounds in place of delavirdine in the patented formulations.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2-20, 22-24, 26, 34, 36-38, 68, 70-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "a rapidly precipitating drug which is a fairly soluble or highly soluble salt form of a poorly soluble free base or free acid that is prone to supersaturating when introduced in water or simulated physiological fluid at body

temperature and more than 90% of it precipitates out within 60 min after coming into contact with said water of simulated physiological fluid at body temperature, with the provisio that the drug is not delavirdine mesylate," in the instant generic claims renders the claims ambiguous.

Specifically for example, if the active drug is the salt of the free base and is a highly soluble salt form of then it is not clear how 90% of it can precipitate out of the water when water itself has a pH of 7. Such end results is simply not achievable if the active ingredient is a highly soluble salt. Therefore, the metes and bounds of the claims are not clear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 2-20, 22-24, 26, 34, 36, 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Makooi-Morehead US Patent 6,238,695 (Makooi) in view of Elger US Patent 4,844,907 (Elger).

Makooi shows the use of lactose; a flow agent such as colloidal silicon dioxide; a superdisintegrants such as croscarmellose and sodium glycolate, and a binder such as microcrystalline. Makooi teaches that such combination of ingredients improves the rate of dissolution and thus the extent of absorption in the GI-track. (col 2, lines 3-7). Accordingly utilizing them and further optimizing their concentrations for desired rate and extent of absorption is well within purview of an ordinary artisan (see col 5, line 40-col 6, line16; col 7, line15-col 8, line33). Makooi also provides the use of compounds that are highly insoluble in water. (col 1, line 63-col 2, line 5). Makooi only fails to use a polymeric binder in his compositions.

Elger's teachings are discussed extensively on the record. Elger provides for various types of drugs within the scope of the instant claim 68 that are highly insoluble in water. Such drugs include diphenhydramine, clindamycin, etc... (see entire col 2). Eldger also teaches the use of polymeric binders such as PVP. (col 3, lines 66-col 4, line 10).

Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to substitute Makooi's drug with other suitable insoluble agents as recited in Elger, because as taught by Makooi's, the ordinary artisan would have had a reasonable expectation of success in improving the rate of dissolution of a insoluble drug and subsequently its extent of absorption in GI track. Further, using any

conventional binder such as PVP or hydroxypropylmethyl cellulose in a tablet formulation of Makooi in place of other art equivalent binders, as taught by Eldger, would have been well within purview of the ordinary skill in the art.

Response to Arguments

5. Applicant's arguments with respect to the rejected claims have been fully considered but are not found persuasive. First, Applicant argues that claim Elger can not be combined with Makooi's teachings because Elger does not advocate the use of lubricants in his formulations. (see Arguments at page 12). As has been argued troughout the prosecution, Examiner responds that the teachings of Elger are not viewed as a direct teaching away from Makooi. The fact that Eldger's use of lubricant has provided an inferior single layer tablet with combination of two active ingredients is not construed as a total bar for application of lubricants in tablet formulations. Generally, "disclosed examples and preferred embodiments do not constitute a teaching which is away from a broader disclosure or nonpreferred embodiments." *In re Susi*, 169 USPQ 423 (CCPA 1971). Applicant appears to selectively ignore what is known to one of ordinary skill in the art with respect to the use of lubricants in a single layer tablets. There are simply no teachings in Eldger or Makooi prohibiting the use of lubricants in single layer tablets.

Eldger is only used as a secondary reference to show the general knowledge in the art about the use of lubricants, binders, and the salt form of active pharmaceutical ingredients in tablet formulations. Here, the modifications of Makooi are merely based on substituting the active drug or known equivalents used in the art to formulate a tablet

dosage form. Such modifications are based on what the state of art of pharmaceutical formulation is and what is construed from the teachings of Makooi by one of ordinary skill in the art. Examiner has taken the position that the modifications described flow naturally from the suggestions of the prior art as all elements of the instant claims are described by the cited references.

In fact, the rejection of record merely uses Elger to show that for purposes of preparing a tablet, the salt forms of rapidly precipitating drugs that fall within the scope of instant claims are essentially functional equivalents to their free base or free acids forms. Note for example the recitation of narcotic analgesics such as hydromorphone or its hydrochloride salts as preferred form. (col 2, lines 4-15).

Furthermore, the use of lubricant in the instant generic claims is in amounts "up to 5 %." This amount includes 0% - 5%. Therefore, Eldger's lack of using lubricants still falls within the scope of the pending claims. Therefore, Examiner concludes that one ordinary skill, upon reading the Elger's reference, would not have been discouraged from using salts forms of compounds in the path set out by Makooi.

Finally, Applicant's assertion that Makooi does not use a fairly soluble or highly soluble salt of poorly soluble free acid is not accurate. Makooi clearly provides for formulations that comprise all suitable type of Efavirnez compounds for pharmaceutical use including its salts forms. Note that at col 3, lines 5-10, Makooi incorporates all the teachings and possible variations of Efavirenz from US Patent 5,519,021 (US '021). The teachings in US '021 is also directed to all suitable salts of Efavirnez (see US '021 at abstract, examples 1-8, claims 1-10).

In fact, Applicant's submitted Declaration of Dr. Walter Morozowich acquiesces to the fact that Efavrirenz can form a salt that is of a free acid encompassed by claim 68. (see Arguments at last line bridging pages 12-13). Therefore, Applicant's arguments that Makooi discourages the use of Efavirnez salts or that Makooi-Morehead only uses poorly soluble free acid form of Efavirnez is not correct.

Declaration by Dr. Morozowich

6. The Declaration under 37 CFR 1.132 filed on May 17, 2005 is insufficient to overcome the rejection of claim 2-20, 22-24, 26, 34, 36, 68 based upon the obviousness rejection as set forth in the last Office action because it refer(s) only to the process described in the above referenced application and not to the individual claims of the application. Thus, there is no showing that the objective evidence of nonobviousness is commensurate in scope with the claims. See MPEP § 716. The rejected claims are not solely directed to active ingredients that are in a free base salt form.

Claim Objections

7. Claims 70-71 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

8. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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